

University of Groningen

Preconceptional Maternal Bile Acids and Birth Weight of Neonates

van Montfoort, Aafke P. A.; Nagy, Ruxandra A.; van Echten-Arends, Jannie; Hoek, Annemieke; Tietge, Uwe J. F.

Published in:
Hepatology communications

DOI:
[10.1002/hep4.1344](https://doi.org/10.1002/hep4.1344)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

van Montfoort, A. P. A., Nagy, R. A., van Echten-Arends, J., Hoek, A., & Tietge, U. J. F. (2019). Preconceptional Maternal Bile Acids and Birth Weight of Neonates. *Hepatology communications*, 3(6), 849-850. <https://doi.org/10.1002/hep4.1344>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Preconceptional Maternal Bile Acids and Birth Weight of Neonates

TO THE EDITOR:

We read with interest the publication by Hagström et al. reporting on pregnancy outcomes in patients with liver cirrhosis.⁽¹⁾ These authors demonstrated in a large general population cohort that maternal liver cirrhosis is associated with an increased risk of (very) low birth weight (BW). This observation might have important implications for offspring health, as low BW is now an established risk factor for metabolic syndrome-related disease later in life.⁽²⁾ Thus, in our view, it would also be relevant and informative to follow up the children born to mothers with liver cirrhosis. The mechanism underlying the observed decreased BW is unclear. However, in patients with liver cirrhosis, circulating bile acids (BA) are commonly elevated. BA are increasingly recognized as endocrine mediators of a diverse range of (patho)physiological functions, including fertility.⁽³⁾

Adding to the observations of Hagström et al., we investigated whether preconceptional alterations in maternal BA are associated with offspring BW. Serum BA were determined at ovum pickup in women undergoing modified natural-cycle *in vitro* fertilization, a procedure close to normal physiology using minimal hormone dosages.⁽³⁾ The institutional

review board waived approval, as only anonymized material/data were used, and patients did not object to use of waste material for research. The study was conducted in accordance with the 1975 Declaration of Helsinki. Sixty singleton deliveries, without clinical/laboratory indications for pre-existing or gestational liver dysfunction, were included. Perinatal data have been published.⁽⁴⁾ A z-score for BW after correction for gestational age, offspring gender, and parity was calculated (<http://www.perinatreg.nl/>). Serum levels of the primary BA chenodeoxycholic and cholic acid (Fig. 1) were significantly correlated with BW z-scores ($r = -0.288$, $P = 0.026$ and $r = -0.274$, $P = 0.034$, respectively). After additional correction for maternal body mass index and smoking in a multivariate regression analysis, cholic and chenodeoxycholic acid were still significant predictors of BW ($\beta = -477.9$, $P = 0.016$ and $\beta = -159.8$, $P = 0.009$, respectively), while total and secondary BA remained unrelated.

In summary, the present analysis demonstrates a significant relationship between higher primary BA in maternal serum at the time of conception and low fetal BW. These novel data extend the observations of Hagström et al. and suggest that even in individuals free of liver disease, maternal BA levels are associated with fetal growth.

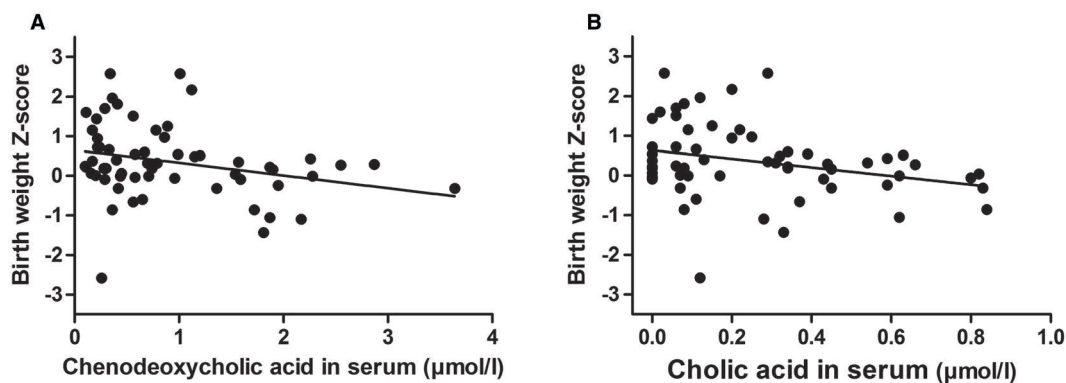


FIG. 1. Correlation between maternal serum levels of primary bile acids at the time of conception and birth weight of the neonate. The graphs plot BW z-score corrected for sex, gestational age at birth, and parity against maternal serum levels of chenodeoxycholic acid (A) or cholic acid (B) at the time of conception.

Acknowledgments: We thank the staff of the Reproductive Medicine Laboratory of the University Medical Center Groningen for collection of patient materials and technical expertise in assisted reproductive medicine and Martijn Koehorst for technical assistance with the bile acid measurements.

Aafke P.A. van Montfoort, M.D., Ph.D.^{1,2*}

Ruxandra A. Nagy, M.D.^{1,3*}

Jannie van Echten-Arends, M.D., Ph.D.¹

Annemieke Hoek, M.D., Ph.D.¹

Uwe J.F. Tietge, M.D., Ph.D.³

¹Department of Obstetrics and Gynecology

Section Reproductive Medicine

University of Groningen

University Medical Center Groningen

Groningen, the Netherlands

²Department of Obstetrics & Gynecology

GROW School for Oncology and Developmental

Biology, Maastricht University Medical Center

Maastricht, the Netherlands

³Department of Pediatrics, Center for Liver

Digestive, and Metabolic Diseases

University of Groningen

University Medical Center Groningen

Groningen, the Netherlands

REFERENCES

- 1) Hagstrom H, Hoijer J, Marschall HU, Williamson C, Heneghan MA, Westbrook RH, et al. Outcomes of pregnancy in mothers with cirrhosis: a national population-based cohort study of 1.3 million pregnancies. *Hepatology* 2018;2:1299-1305.
- 2) Barker DJ. The developmental origins of adult disease. *J Am Coll Nutr* 2004;23(6 Suppl):588S-595S.
- 3) **Nagy RA, van Montfoort AP**, Dikkers A, van Echten-Arends J, Homminga I, Land JA, et al. Presence of bile acids in human follicular fluid and their relation with embryo development in modified natural cycle IVF. *Hum Reprod* 2015;30:1102-1109.
- 4) Pelinck MJ, Keizer MH, Hoek A, Simons AH, Schelling K, Middelburg K, et al. Perinatal outcome in singletons after modified natural cycle IVF and standard IVF with ovarian stimulation. *Eur J Obstet Gynecol Reprod Biol* 2010;148:56-61.

Author names in bold designate shared co-first authorship.

**These authors contributed equally to this work.*

Supported by the Netherlands Organization for Scientific Research (VIDI grant 917-56-358 to U.J.F.T.).

© 2019 The Authors. *Hepatology Communications* published by Wiley Periodicals, Inc., on behalf of the American Association for the Study of Liver Diseases. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

View this article online at wileyonlinelibrary.com.

DOI 10.1002/hep4.1344

Potential conflict of interest: Dr. Hoek received grants from Ferring.